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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/587,111	06/02/00	CURTIS R	MNI-062CP2DV

000959
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HM12/1031

EXAMINER	
ULM, J	

ART UNIT	PAPER NUMBER
1646	9

DATE MAILED: 10/31/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/587,111	Curtis
Examiner	**Art Unit**
John Ulm	1646

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Oct 9, 2001*.

2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-26* is/are pending in the application.

4a) Of the above, claim(s) *1-19 and 22-26* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *20 and 21* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☐ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 5
18) ☐ Interview Summary (PTO-413) Paper No(s). _____
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other:

1) Claims 1 to 26 are pending in the instant application. Claims 1 to 19 and 24 to 26 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in Paper No. 8.

2) Claims 20 and 21 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. A properly dependant claim can not conceivably be infringed without infringing any of the claims from which it depends. These claims can be infringed by a process which employs a cell that naturally expresses hVR-2 and such a process would not infringe the "isolated" polypeptide of claim 10, from which these claims depend. See M.P.E.P. 608.01(n)III.

3) This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 C.F.R. § 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 C.F.R. § 1.821 through 1.825. Specifically, no paper copy of a "Sequence Listing" has been provided in the instant application. Applicant needs to provide an initial paper copy of a "Sequence Listing" which includes all of the sequences that are present in the instant application and encompassed by these rules and a statement that the content of the paper and computer readable copies of the "Sequence Listing" in the instant application are the same and, where applicable, include no new

matter, as required by 37 C.F.R. §§ 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d). For rules interpretation Applicant may call (703) 308-1123. See M.P.E.P. 2422.04.

4) The instant specification does not comply with 37 C.F.R. § 1.84(U)(1), which states that partial views of a drawing which are intended to form one complete view, whether contained on one or several sheets, must be identified by the same number followed by a capital letter. Figure 1 of the instant application, for example, is presented on four separate panels. The four sheets of drawings which are labeled " Figure 1" in the instant specification should be renumbered "Figures 1A, 1B, 1C and 1D". Applicant is reminded that once the drawings are changed to meet the separate numbering requirement of 37 C.F.R. § 1.84(U)(1), Applicant is required to file an amendment to change the Brief Description of the Drawings and the rest of the specification accordingly.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5) Claims 20 and 21 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the practice of a method of identifying a ligand which binds to a receptor protein comprising the amino acid sequence presented in SEQ ID NO:5 of the instant specification, does not reasonably provide enablement for the practice of a binding assay which employs a protein having anything less than the entire amino acid sequence presented in SEQ ID NOs:5, 11 or 20. The specification does not enable any person skilled in the art to which

it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The instant specification discloses that a polypeptide having the amino acid sequence presented in SEQ ID NO:5 of the instant specification is a naturally occurring protein which is presumably a member of the family of proteins known as G protein-coupled receptors and, potentially, a vanilloid receptor which is involved with the transmission of sensations of pain. The protein encoded thereby can be used to identify ligands which may be potentially pharmacologically relevant. The information derived therefrom is only relevant in so far as it is applicable to the native protein. Because the information derived from such an assay is only relevant in so far as it is applicable to the native protein and the instant specification does not identify those amino acid residues in the amino acid sequence of SEQ ID NO:5 which are essential for biological activity and structural integrity of a hVR-2 protein and those residues which are either expendable or substitutable, a practitioner can not make and use a polypeptide lacking that entire sequence with any reasonable expectation that the altered protein would respond in an authentic manner. In the absence of such structure-function information a practitioner would have to resort to a substantial amount of undue experimentation in the form of insertional, deletional and substitutional mutation analysis of over 760 amino acid residues before they could even begin to rationally design an hVR-2 polypeptide having other than a natural amino acid sequence and which responds in a binding assay in a manner which is representative of the native protein. If fact, the instant specification does not provide a method through which an

artisan can determine if a derivative of the disclosed protein retains functionality because the instant specification discloses neither a demonstrated ligand for the instant receptor or the pathway through which it has been shown to signal. A receptor, by definition, must bind a ligand and transduce a signal. To determine if a derivative of a receptor has retained its function an artisan must be able to measure both of these activities. Since the instant specification does not identify a ligand which has been demonstrated to bind to the disclosed protein, it is not possible to determine if ligand-binding is retained.

The disclosure in the instant specification that the hVR-2 protein described therein is structurally related to the capsaicin receptor VR-1 does not support a conclusion that hVR-2 will bind capsaicin. Proteins belonging to the family of G protein-coupled receptors bind a variety of structurally unrelated compounds ranging from simple compounds like glutamate, glycine, dopamine, serotonin, somatostatin and epinephrin to complex molecules such as interleukin-8. However, because the differences between the amino acid sequence of the hVR-2 protein of the instant invention and that of hVR-1 are greater than the similarities, one would not conclude that these two proteins bind the same spectrum of ligands or modulate the same cellular processes. It was well known in the art prior to the making of the instant invention that receptor proteins belonging to the same structural family, such as the G protein-coupled adrenergic and dopamine receptors, could share substantial amino acid sequence similarity and still modulate completely different physiological processes in response to structurally related but different ligands. The administration of dopamine to an individual certainly has a profoundly different effect than the

administration of adrenaline even though these two compounds are structurally related and the receptors for these two related compounds share substantial structural as well as amino acid sequence similarities. One would not reasonably conclude, based upon the limited amino acid sequence similarity between the hVR-2 protein of the instant invention and hVR-1 that the effects of clinical administration of an agonist to one of these receptors would be predictive of the clinical effects of administering an agonist to the other. Therefore, one can not predict to which ligand the instant receptor will bind by reviewing its amino acid sequence. Further, it is well known in the that G protein-coupled receptors signal through a variety of different pathways, depending upon the type of G protein to which a particular receptor is coupled.

The instant application does not provide even a single example of a receptor protein other than the three naturally occurring receptor proteins that are disclosed in the instant application as SEQ ID NO:5, SEQ ID NO:11 and SEQ ID NO:20. *In re Fisher*, 427 F.2d 833, 166 USPQ 18 (CCPA 1970), held that:

> "Inventor should be allowed to dominate future patentable inventions of others where those inventions were based in some way on his teachings, since such improvements while unobvious from his teachings, are still within his contribution, since improvement was made possible by his work; however, he must not be permitted to achieve this dominance by claims which are insufficiently supported and, hence, not in compliance with first paragraph of 35 U.S.C. 112; that paragraph requires that scope of claims must bear a reasonable correlation to scope of enablement provided by specification to persons of ordinary skill in the art; in cases involving predictable factors, such as mechanical or electrical elements, a single embodiment provides broad enablement in the sense that, once imagined, other

embodiments can be made without difficulty and their performance characteristics predicted by resort to known scientific law; in cases involving unpredictable factors, such as most chemical reactions and physiological activity, scope of enablement varies inversely with degree of unpredictability of factors involved."

In the absence of both working examples of intentionally altered VR-2 proteins and information on the ligand and signaling pathway of the disclosed protein an artisan could not alter a single amino acid residue in SEQ ID NO:5 with any confidence that the resulting protein will function in a manner that is representative of its native analog and the instant specification does not disclose how to use information that is obtained from an assay which employs a protein that does not function in a manner that is representative of its native analog.

Further, claim 21 encompasses a method which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. This claim encompasses an assay which requires a practitioner to measure hVR-2 activity in response to the binding of a ligand to that receptor. To practice the claimed assay one must be able to measure a signal which is transduced by the ligand activation of an hVR-2 protein and the instant application does not identify a specific cellular signal which has been shown to be modulated by the binding of a ligand to a receptor of the instant invention. As stated above, it is well established in the art that different members of the G protein-coupled receptor family can signal through various different pathways. Since the instant specification does not disclose a pathway through which the disclosed protein is known to signal

then a practitioner would be incapable of practicing the claimed method without resorting to the substantial undue experimentation of first discovering a ligand for the disclosed receptor and then discovering a signaling pathway through which that receptor signals when bound by that ligand.

6) Claims 20 and 21 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. There is absolutely no written description in the instant specification of an allelic variant of a protein comprising the amino acid sequence presented in SEQ ID NO:5 of the instant application. In the decision of *The Regents of the University of California v. Eli Lilly and Company,* 43 USPQ2d 1398 (CAFC 1997), the court held that:

> "To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." Lockwood v. American Airlines, Inc. , 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); In re Gosteli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood , 107 F.3d at 1572, 41 USPQ2d at 1966.
>
> An adequate written description of a DNA, such as the cDNA of the recombinant plasmids and microorganisms of the '525 patent, "requires a precise definition, such as by

structure, formula, chemical name, or physical properties," not a mere wish or plan for obtaining the claimed chemical invention. Fiers v. Revel , 984 F.2d 1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993). Accordingly, "an adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself." Id. at 1170, 25 USPQ2d at 1606.

Whereas the instant specification provides a detailed description of a single isolated DNA encoding particular protein having very specific physical and structural properties, the instant specification does not provide a structural formula which is definitive of all, or even one allelic variant of that one protein. The instant specification also fails to provide "a precise definition, such as by structure, formula, chemical name, or physical properties," of the genus of isolated hVR-2 polypeptides to be employed ion the binding assay of these claims.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

7) Claims 20 and 21 are rejected under 35 U.S.C. 102(a) as being clearly anticipated by each of the Julius et al. (WO 99/37675) and Davis et al. (WO 99/37765) publications. SEQ ID NO:5 of the instant application is identical to SEQ ID NO:36 of Julius et al. and SEQ ID NO:2 of Davis et al. The claimed assay was described on pages 23 and 24 of Julius et al. and on page 13 of Davis et al.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to John D. Ulm whose telephone number is (703) 308-4008. The examiner can normally be reached on Monday through Friday from 9:00 AM to 5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached at (703) 308-6564.

Official papers filed by fax should be directed to (703) 308-4242 or (703) 872-9306. Official responses under 37 C.F.R. § 1.116 should be directed to (703) 872-9307.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

JOHN ULM
PRIMARY EXAMINER
GROUP 1800